Studies on the Constituents of *Viburnum* Species. XIX.[1)] Six New Triterpenoids from *Viburnum dilatatum* THUNB.

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Six new triterpenoids, viburnudienone B_1 methyl ester (1), viburnudienone B_2 methyl ester (2), viburnudienone H_1 (3), viburnudienone H_2 (4), viburnenone B_1 methyl ester (5) and viburnenone B_2 methyl ester (6), were isolated from the leaves of *Viburnum dilatatum* (Caprifoliaceae). Their structures were established by extensive spectroscopic studies.

Key words *Viburnum dilatatum*; Caprifoliaceae; triterpene; dammarane; viburnudienone; viburnenone

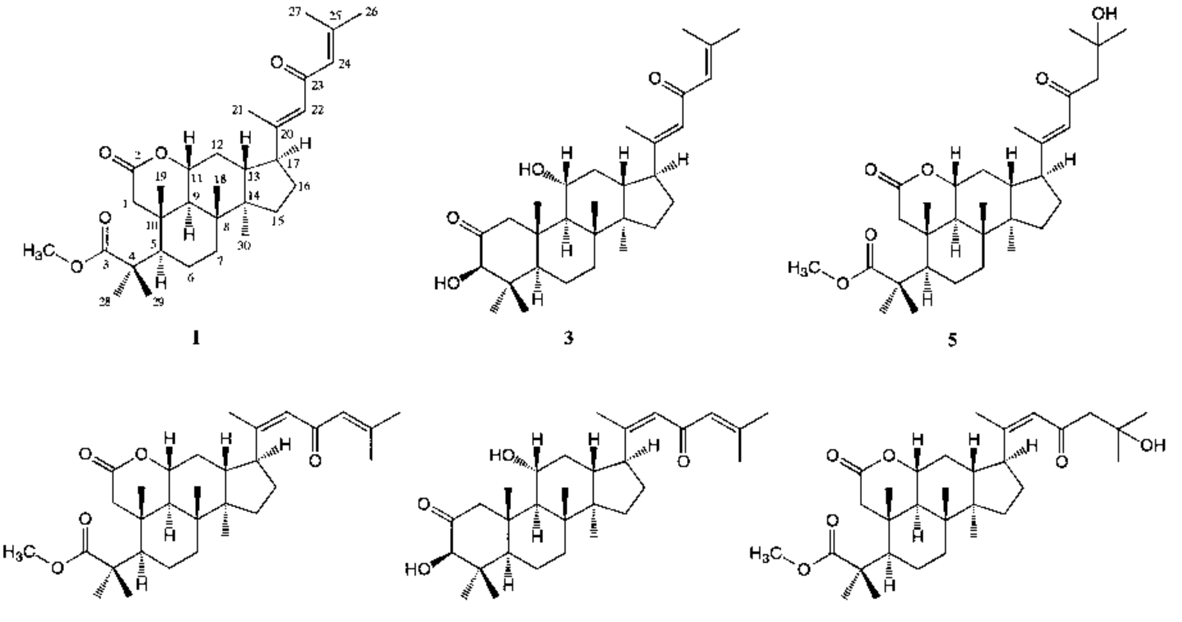
We have recently reported the isolation of eleven, new class, modified dammarane-type triterpenoids, viburnols A—K, from the $CHCl_3$ extract of the leaves of *Viburnum dilatatum*.[1,2)] In the present study, six new dammarane-type triterpenoids, viburnudienone B_1 methyl ester (**1**), viburnudienone B_2 methyl ester (**2**), viburnudienone H_1 (**3**), viburnudienone H_2 (**4**), viburnenone B_1 methyl ester (**5**) and viburnenone B_2 methyl ester (**6**), were isolated. This paper deals with the structural elucidation of these compounds.

Results and Discussion

Viburnudienone B_1 methyl ester (**1**) was obtained as an amorphous powder, $[\alpha]_D$ +26.4°. The molecular formula was determined to be $C_{31}H_{46}O_5$ by high-resolution (HR)-MS. The ^{1}H- and ^{13}C-NMR spectra of **1** were very similar to those of viburnol B methyl ester,[2)] except for the signals due to the side chain part (C_{20}—C_{27}). As regarding the side chain part, the spectral data revealed the presence of a dienone [269 nm; 1668, 1621 cm^{-1}; δ_H 6.05 (1H, m, H-24), 6.01 (1H, br s, H-22), δ_C 191.4 (s, C-23), 158.5 (s, C-20), 154.7 (s, C-25), 126.3 (d, C-22), 126.0 (d, C-24)] and three olefinic methyl groups [δ_H 2.17 (3H, d, J=1.2 Hz, H-27), 2.10 (1H, d, J=1.0 Hz, H-21), 1.89 (1H, d, J=1.2 Hz, H-26)].

Viburnudienone B_2 methyl ester (**2**) was also obtained as an amorphous powder, $[\alpha]_D$ +17.6°. The molecular formula was determined to be $C_{31}H_{46}O_5$ by HR-MS. The ^{1}H- and ^{13}C-NMR spectra of **2** were very similar to those of **1**, except for the side chain moiety. These spectral data indicated that **1** and **2** were dammarane-type triterpenoids having a 20,24-diene-23-one type side chain, respectively, and differed only at the stereochemistry of the double bond at C-20. The stereochemistry of the C-20, 22 double bond in **1** and **2** was determined to be *E* and *Z* configurations by the nuclear Overhauser effect (NOE) difference spectra (NOE: **1**; H-22/H-17, **2**; H-22/CH_3-21), respectively. On the basis of the above evidence, **1** and **2** are clearly established as depicted in the formulas.

Viburnudienones H_1 (**3**) and H_2 (**4**) were isolated as an amorphous powder, $[\alpha]_D$ +50.0° and +44.4°, respectively. The ^{1}H- and ^{13}C-NMR spectra of **3** and **4** were very similar to those of viburnol H,[1)] except for the signals due to the side chain. As regarding the side chain moieties of **3** and **4**, the



1 3 5

2 4 6

Chart 1

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Table 1. ^{13}C-NMR Spectral Data (67.8 MHz, $CDCl_3$)

C	**1**	**2**	**3**	**4**	**5**	**6**
1	48.2	48.2	55.9	55.9	48.2	48.1
2	169.7	169.8	212.1	212.2	169.6	169.7
3	179.0	178.9	82.4	82.4	179.0	179.0
4	45.4	45.4	45.3	45.3	45.4	45.4
5	55.3	55.2	55.4	55.4	55.3	55.2
6	19.9	19.9	18.3	18.3	19.9	19.9
7	35.2	35.2	35.7	35.8	35.2	35.2
8	39.7	39.7	41.4	41.3	39.7	39.7
9	47.6	47.5	55.1	55.3	47.6	47.5
10	38.2	38.2	44.9	44.9	38.2	38.2
11	77.2	77.3	70.4	70.6	76.8	77.1
12	32.5	32.5	37.2	37.2	32.5	32.6
13	43.8	44.0	43.6	43.9	43.9	44.1
14	49.3	49.3	49.5	49.6	49.4	49.4
15	31.4	31.4	31.5	31.7	31.4	31.4
16	27.7	27.0	27.9	27.2	27.7	27.1
17	50.5	40.5	51.2	41.1	50.6	40.9
18	15.4	15.4	16.4	16.4	15.4	15.5
19	17.9	17.8	17.7	17.7	17.9	17.9
20	158.5	157.7	158.4	158.6	161.4	161.0
21	16.5	20.2	16.5	20.2	16.9	20.4
22	126.3	128.8	126.3	128.6	124.3	126.9
23	191.4	191.0	191.4	191.2	202.2	202.0
24	126.0	126.6	125.7	126.4	54.2	54.2
25	154.7	154.5	154.5	154.2	70.0	69.9
26	27.8	27.7	27.8	27.7	29.5	29.5
27	20.6	20.6	20.6	20.6	29.4	29.4
28	22.7$^{a)}$	22.7$^{b)}$	29.5	29.5	22.7$^{c)}$	22.7$^{d)}$
29	27.9$^{a)}$	27.9$^{b)}$	16.6	16.6	27.9$^{c)}$	28.0$^{d)}$
30	15.8	16.1	15.9	16.2	15.8	16.0
$COO\underline{C}H_3$	52.0	52.0	—	—	52.0	52.0

a—d) Signals may be interchanged in each column.

spectral data were almost the same as those of **1** and **2**, respectively. The gross structures of **3** and **4** were proved by heteronuclear multiple bond correlation (HMBC) and nuclear Overhauser enhancement and exchange spectroscopy (NOESY) spectra. Thus, viburnudienones H_1 (**3**) and H_2 (**4**) are clearly established as depicted in the formulas.

Viburnenones B_1 methyl ester (**5**) and B_2 methyl ester (**6**) were isolated as an amorphous powder, $[\alpha]_D$ +26.0° and +12.5°, respectively. Both of their molecular formulas were determined to be $C_{31}H_{48}O_6$ by HR-MS. The ^{1}H- and ^{13}C-NMR spectra of **5** and **6** lacked the signals due to a trisubstituted double bond at C-24, 25. Instead, they showed the characteristic signals of a hydroxy-bearing quaternary carbon [**5**: δ_H 4.17 (1H, s, HO-25), δ_C 70.0 (s, C-25), **6**: δ_H 4.14 (1H, s, HO-25), δ_C 69.9 (s, C-25)] and a methylene group linked to a carbonyl group [**5**: δ_H 2.60 (2H, s, H-24), δ_C 54.2 (t, C-24), **6**: δ_H 2.57 (2H, s, H-24), δ_C 54.2 (t, C-24)], respectively. These findings suggested that **5** and **6** possessed a 25-hydroxy-20-en-23-one type side chain, respectively. The stereochemistry of the C-20, 22 double bond in **5** and **6** was determined to be *E* and *Z* configurations by comparison of ^{1}H- and ^{13}C-NMR spectra with **1** and **2**, respectively. Thus, the structures of **5** and **6** were established to be as depicted in the formulas.

Experimental

^{1}H- and ^{13}C-NMR spectra were recorded with a JEOL JNM-EX 270 spectrometer (270 and 67.8 MHz, respectively, TMS as int. standard). UV spectra were recorded with a Beckman DU-64 spectrophotometer. IR spectra were recorded with a Perkin-Elmer FT-IR 1725X infrared spectrophotometer. MS were recorded with a JEOL JMS-DX 303 mass spectrometer. Column chromatography was carried out on Kieselgel 60 (Merck; 230—400 mesh), Cosmosil 75C_{18}-OPN (Nacalai Tesque). Preparative HPLC was carried out on Tosoh HPLC system using Cosmosil 5C18-AR (Nacalai Tesque, 10 mm i.d.×25 cm) and TSK gel OH-120 (Tosoh Co., 7.8 mm i.d.×30 cm) columns with UV detector.

Extraction and Isolation Fresh leaves of *V. dilatatum* (4.4 kg) were extracted with MeOH. The MeOH extract was concentrated under reduced pressure and the residue was suspended in a small excess of water. This suspension was successively extracted with $CHCl_3$, Et_2O, AcOEt and *n*-BuOH. The $CHCl_3$ soluble fraction was concentrated under reduced pressure to produce a residue (92.5 g). This residue was chromatographed on a silica gel column using *n*-hexane–Me_2CO (4 : 1) and eluate was separated into four fractions (frs. 1—4). Fraction 3 was rechromatographed on a 75C_{18} open column using MeOH–H_2O (3 : 1) and the eluate was separated into six fractions (frs. 3-1—3-6). Fraction 3-2 was subjected to prep. HPLC [5C18-AR column; MeOH–H_2O (5 : 1), flow rate: 1.5 ml/min, detection: 270 nm] to give compounds **1** (5.0 mg), **2** (5.0 mg), **3** (1.2 mg) and **4** (1.0 mg). Fraction 3-3 was subjected to prep. HPLC [OH-120 column; *n*-hexane–acetone (5 : 1), *n*-hexane–AcOEt (3 : 1), flow rate: 0.75, 1.5 ml/min, detection: 240 nm] to give compounds **5** (2.0 mg) and **6** (0.6 mg).

Viburnudienone B_1 Methyl Ester (1) An amorphous powder, $[\alpha]_D$ +26.4° (c=0.5, $CHCl_3$). EI-MS *m/z*: 498 $[M]^+$. HR-MS *m/z*: 498.3363 (M^+, Calcd for $C_{31}H_{46}O_5$; 498.3345). UV λ_{max}^{MeOH} nm (log ε): 269.0 (4.21). IR ν ($CHCl_3$) cm^{-1}: 2954, 2880, 1719, 1668, 1621. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 6.05 (1H, m, 24-H), 6.01 (1H, br s, 22-H), 4.37 (1H, ddd, J=11.9, 11.4, 5.0 Hz, 11-H), 3.70 (3H, s, $COOCH_3$), 2.50 (1H, d, J=16.7 Hz, 1-H_β), 2.38 (1H, m, 17-H), 2.28 (1H, d, J=16.7 Hz, 1-H_α), 2.17 (3H, d, J=1.2 Hz, 27-CH_3), 2.10 (3H, d, J=1.0 Hz, 21-CH_3), 1.89 (3H, d, J=1.2 Hz, 26-CH_3), 1.78 (1H, d, J=11.9 Hz, 9-H), 1.24, 1.22 (3H each, s, 28, 29-CH_3), 1.19 (3H, s, 19-CH_3), 1.04 (3H, s, 18-CH_3), 0.97 (3H, s, 30-CH_3). ^{13}C-NMR (67.8 MHz, $CDCl_3$): Table 1.

Viburnudienone B_2 Methyl Ester (2) An amorphous powder, $[\alpha]_D$ +17.6° (c=0.5, $CHCl_3$). EI-MS *m/z*: 498 $[M]^+$. HR-MS *m/z*: 498.3331 (M^+, Calcd for $C_{31}H_{46}O_5$; 498.3345). UV λ_{max}^{MeOH} nm (log ε): 269.0 (4.07). IR ν ($CHCl_3$) cm^{-1}: 2954, 2880, 1719, 1668, 1620. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 6.08 (1H, t, J=1.2 Hz, 22-H), 6.02 (1H, t, J=1.2 Hz, 24-H), 4.33 (1H, ddd, J=11.8, 11.4, 5.0 Hz, 11-H), 4.13 (1H, ddd, J=11.1, 10.5, 6.3 Hz, 17-H), 3.70 (3H, s, $COOCH_3$), 2.48 (1H, d, J=17.0 Hz, 1-H_β), 2.25 (1H, d, J=17.0 Hz, 1-H_α), 2.14 (3H, d, J=1.2 Hz, 27-CH_3), 1.88 (3H, d, J=1.2 Hz, 26-CH_3), 1.81 (3H, d, J=1.2 Hz, 21-CH_3), 1.77 (1H, d, J=11.8 Hz, 9-H), 1.24, 1.22 (3H each, s, 28, 29-CH_3), 1.18 (3H, s, 19-CH_3), 1.03 (3H, s, 18-CH_3), 1.02 (3H, s, 30-CH_3). ^{13}C-NMR (67.8 MHz, $CDCl_3$): Table 1.

Viburnudienone H_1 (3) An amorphous powder, $[\alpha]_D$ +50.0° (c=0.1, $CHCl_3$). EI-MS *m/z*: 470 $[M]^+$. HR-MS *m/z*: 470.3437 (M^+, Calcd for $C_{30}H_{46}O_4$; 470.3396). UV λ_{max}^{MeOH} nm (log ε): 269.0 (4.03). IR ν ($CHCl_3$) cm^{-1}: 3472, 2956, 1707, 1669, 1620. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 6.06 (1H, t, J=1.2 Hz, 24-H), 6.02 (1H, br s, 22-H), 3.99 (1H, m, 11-H), 3.90 (1H, s, 3-H), 3.50 (1H, d, J=13.0 Hz, 1-H_β), 2.32 (1H, m, 17-H), 2.25 (1H, d, J=13.0 Hz, 1-H_α), 2.17 (3H, d, J=1.2 Hz, 27-CH_3), 2.10 (3H, d, J=1.2 Hz, 21-CH_3), 1.89 (3H, d, J=1.2 Hz, 26-CH_3), 1.71 (1H, d, J=10.4 Hz, 9-H), 1.19 (3H, s, 28-CH_3), 1.00 (9H, s, 18, 19, 30-CH_3), 0.71 (3H, s, 29-CH_3). ^{13}C-NMR (67.8 MHz, $CDCl_3$): Table 1.

Viburnudienone H_2 (4) An amorphous powder, $[\alpha]_D$ +44.4° (c=0.1, $CHCl_3$). EI-MS *m/z*: 470 $[M]^+$. HR-MS *m/z*: 470.3359 (M^+, Calcd for $C_{30}H_{46}O_4$; 470.3396). UV λ_{max}^{MeOH} nm (log ε): 269.0 (3.99). IR ν ($CHCl_3$) cm^{-1}: 3475, 2955, 1707, 1670, 1620. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 6.06 (1H, t, J=1.3 Hz, 22-H), 6.03 (1H, d, J=1.3 Hz, 24-H), 4.06 (1H, m, 17-H), 3.98 (1H, m, 11-H), 3.90 (1H, s, 3-H), 3.51 (1H, d, J=12.9 Hz, 1-H_β), 2.23 (1H, d, J=12.9 Hz, 1-H_α), 2.14 (3H, d, J=1.3 Hz, 27-CH_3), 1.88 (3H, d, J=1.3 Hz, 26-CH_3), 1.81 (3H, d, J=1.3 Hz, 21-CH_3), 1.70 (1H, d, J=10.6 Hz, 9-H), 1.19 (3H, s, 28-CH_3), 1.04, 0.996, 0.989 (9H, s, 18, 19, 30-CH_3), 0.70 (3H, s, 29-CH_3). ^{13}C-NMR (67.8 MHz, $CDCl_3$): Table 1.

Viburnenone B_1 Methyl Ester (5) An amorphous powder, $[\alpha]_D$ +26.1° (c=0.2, $CHCl_3$). EI-MS *m/z*: 516 $[M]^+$. HR-MS *m/z*: 516.3448 (M^+, Calcd for $C_{31}H_{48}O_6$; 516.3450). UV λ_{max}^{MeOH} nm (log ε): 246.0 (4.06). IR ν ($CHCl_3$) cm^{-1}: 3424, 2963, 1719, 1660, 1602. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 5.99 (1H, s, 22-H), 4.37 (1H, ddd, J=11.7, 11.4, 5.0 Hz, 11-H), 4.17 (1H, s, 25-OH), 3.71 (3H, s, $COOCH_3$), 2.60 (2H, s, 24-H_2), 2.51 (1H, d, J=17.3 Hz, 1-H_β), 2.38 (1H, m, 17-H), 2.29 (1H, d, J=17.3 Hz, 1-Hα), 2.10 (3H, s, 21-CH_3), 1.98 (1H, m, 12-H_β), 1.78 (1H, d, J=11.7 Hz, 9-H), 1.26 (6H, s, 26, 27-CH_3), 1.24, 1.22 (3H each, s, 28, 29-CH_3), 1.20 (3H, s, 19-CH_3), 1.05 (3H, s, 18-CH_3), 0.97 (3H, s, 30-CH_3). ^{13}C-NMR (67.8 MHz, $CDCl_3$): Table 1.

Viburnenone B_2 Methyl Ester (6) An amorphous powder, $[\alpha]_D$ +12.5°

(c=0.06, $CHCl_3$). EI-MS *m*/*z*: 516 $[M]^+$. HR-MS *m*/*z*: 516.3486 (M^+, Calcd for $C_{31}H_{48}O_6$; 516.3450). UV λ_{max}^{MeOH} nm (log ε): 247.0 (3.96). IR ν ($CHCl_3$) cm^{-1}: 3441, 2963, 1719, 1658, 1602. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 6.06 (1H, d, *J*=1.2 Hz, 22-H), 4.33 (1H, ddd, *J*=11.5, 11.3, 4.8 Hz, 11-H), 4.14 (1H, s, 25-HO), 4.06 (1H, ddd, *J*=11.2, 10.5, 6.7 Hz, 17-H), 3.70 (3H, s, $COOCH_3$), 2.57 (2H, s, 24-H_2), 2.49 (1H, d, *J*=17.2 Hz, 1-H_β), 2.26 (1H, d, *J*=17.2 Hz, 1-H_α), 1.83 (3H, d, *J*=1.2 Hz, 21-CH_3), 1.78 (1H, d, *J*=11.5 Hz, 9-H), 1.24 (6H, s, 26, 27-CH_3), 1.23, 1.22 (3H each, s, 28,29-CH_3),1.18 (3H, s, 19-CH_3), 1.04 (3H, s, 18-CH_3), 1.03 (3H, s, 30-CH_3). ^{13}C-NMR (67.8 MHz, $CDCl_3$): Table 1.

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References

1) Machida K., and Kikuchi M., *Chem. Pharm. Bull.*, **45**, 1928—1931 (1997).
2) Machida K., and Kikuchi M., *Chem. Pharm. Bull.*, **45**, 1589—1592 (1997).